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PATTERSON, THUENTE, SKAAR & CHRISTENSEN, P.A.
4800 IDS CENTER
80 SOUTH 8TH STREET
MINNEAPOLIS, MN 55402-2100

EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 06/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/652,814	UNGER, GRETCHEN M.	
	Examiner	Art Unit	
	Ileana Popa	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *66-95,97-109,111-116,118,119,122-124,126,127,133 and 134* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66,67,87-94,101,133 and 134* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 68-86,95,97-100,102-109,111-116,118,119,122-124,126 and 127.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of the invention of Group II, drawn to a composition comprising a surfactant associated with a bioactive component and a shell surrounding the association of bioactive component and surfactant, wherein the shell comprises at least one biocompatible polymer that provides specific cellular or tissue uptake and of proteinaceous material as a biocompatible polymer, in the reply filed on 05/24/2006 is acknowledged. It is noted that the Applicant did not provide any grounds for the traversal of restriction requirement. The requirement is still deemed proper and is therefore made FINAL.

Claims 1-65, 96, 110, 117, 120-121, 125, and 128-132 have been cancelled. New claims 133 and 134 have been added. Claims 66, 67, 87-95, and 97-102 have been amended. No new matter was introduced by these amendments or by the addition of the new claims 133 and 134.

The Applicant requests the withdrawal of claims 66, 68-86, and 103-132. However, it is noted that claim 66 has been amended to include the limitation of claim 67 and claim 67 is now dependent on claim 66. Accordingly, claim 66 is included in Group II. Similarly, claims 133 and 134 are included in Group II.

Claims 68-86 and 103-109, 111-116, 118, 119, 122-124, 126, and 127 are withdrawn from further consideration as per Applicants request filed on 05/24/2006 (page 2).

Claims 95, 97-100, and 102 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), or for being drawn to nonelected species, there being no allowable generic or linking claim.

Claims 66, 67, 87-94, 101, 133, and 134 are under examination.

Specification

2. The substitute specification filed 04/21/2006 has been entered.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees.

A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 66, 67, 87, 88, 90, 92-94, 101, 133, and 134 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, and 8 of copending Application No. 10/378,044. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are obvious variants.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The instant claims are drawn to a composition of a plurality of particles comprising a core provided by a bioactive component associated with a surfactant having an HLB value of less than about 6.0, and a shell surrounding the association of the bioactive component and the surfactant, wherein the shell comprises at least one biocompatible polymer and wherein the biocompatible polymer provides specific cellular or tissue uptake; and the particles have an average diameter of less than 50 nm as measured by atomic force microscopy after drying of the particles (claim 66). The biocompatible polymer comprises a macromolecule such as a proteinaceous material (claims 66, 101, 133, and 134), the surfactant has a HLB of less than 5.0 (claim 88) and can be a non-ionic (claim 87) or is selected from the group recited in claim 90, and the composition further comprises a biocompatible oil (claim 92), a water-miscible solvent (claim 93) or a cation selected from the group recited in claim 94. The instant claims embrace the following embodiments: particles with an average diameters of less than 50 nm, the particle comprising bioactive component, a surfactant with an HLB less than

6.0 and a biocompatible polymer that provides specific cellular uptake, wherein the biocompatible polymer is a proteinaceous material such as tenascin.

The application claims are drawn a collection of particles having a biocoactive component such as nucleic acids (i.e., macromolecules), a surfactant with an HLB less than 6.0, a biocompatible polymer, and a cell recognition component having affinity for a cell recognition target such as an integrin; the average diameter of the particles is less than 200 nm as measured by atomic force microscopy after drying of the particles (claims 1, 2, and 8). The specification defines that the surfactant can be a non-ionic surfactant or 2,4,7,9-tetramethyl-5-decyn-4,7-diol (i.e., a surfactant that has an HLB of less than 5.0), as recited in the instant claims 87 and 90, the polymer is a biocompatible polymer that surrounds the association between the bioactive component and the surfactant (i.e., the polymer forms a shell surrounding the association between the bioactive component and the surfactant), the particles may have an average diameter of less than 200, 100 or 50 nm, and that the composition further comprises one of the cations recited in the instant claim 94 or a water-miscible solvent (paragraphs 0040, 0041, 0166, 0168). With respect to the limitation of the biocompatible polymer providing specific cellular or tissue uptake, the specification discloses that the biocompatible polymer can be tenascin that provides targeted cellular uptake via integrin receptors on the cell surface, i.e., the particles have a ligand that targets a receptor for tenascin (paragraphs 0071, 0121). With respect to the limitation of a biocompatible oil, the specification discloses that the particles can comprise a pharmaceutically acceptable carrier based on oil, i.e., a biocompatible oil (paragraph 0161). Thus, the application

claims 1, 2, and 8 anticipate the instant claims 66, 67, 87, 88, 90, 92-94, 101, 133, and 134. Since the claims of the Application No. 10/378,044 embrace all limitation of the instant claims, the application claims and the instant claims are obvious variants of one another.

Claims 66, 87, 88, 90, 92-94, 101, 133, and 134 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10 and 13 of copending Application No. 10/958,999. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are obvious variants.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The instant claims are drawn to a composition of a plurality of particles comprising a core provided by a bioactive component associated with a surfactant having an HLB value of less than about 6.0, and a shell surrounding the association of the bioactive component and the surfactant, wherein the shell comprises at least one biocompatible polymer and wherein the biocompatible polymer provides specific cellular or tissue uptake; and the particles have an average diameter of less than 50 nm as measured by atomic force microscopy after drying of the particles (claim 66). The biocompatible polymer comprises a macromolecule such as a proteinaceous material (claims 66, 101, 133, and 134), the surfactant has a HLB of less than 5.0 (claim 88) and can be a non-ionic (claim 87) or is selected from the group recited in claim 90, and the

composition further comprises a biocompatible oil (claim 92), a water-miscible solvent (claim 93) or a cation selected from the group recited in claim 94. The instant claims embrace the following embodiments: particles with an average diameters of less than 50 nm, the particle comprising bioactive component, a surfactant with an HLB less than 6.0 and a biocompatible polymer that provides specific cellular uptake, wherein the biocompatible polymer is a proteinaceous material such as tenascin. The specification defines that the bioactive component can be an antisense DNA (paragraph 0108).

The application claims recite a collection of particles comprising an agent, a surfactant molecule having an HLB of less than 6.0, a polymer soluble in aqueous solution, wherein the collection of particles has an average diameter of less than about 100 nm as measured by atomic force microscopy after drying and wherein the agent is a modified anti-sense nucleic acid directed against protein kinase CK2beta (claim 10). The collection of particles further comprises a cell recognition agent (claim 13). The specification defines that the surfactant can be a non-ionic surfactant or 2,4,7,9-tetramethyl-5-decyn-4,7-diol, i.e., a surfactant with an HLB of less that 5.0, the particles further comprise water-miscible solvents or one of the cations recited in claim 94, and the polymer can be tenascin (paragraphs 0047, 0048, 0148, 0150, 0155, 0164, 0174).

With respect to the limitation of a biocompatible oil, the specification discloses that the particles can comprise a pharmaceutically acceptable carrier based on oil, i.e., a biocompatible oil (paragraph 056). Thus, the application claims 10 and 13 anticipate the instant claims 66, 67, 87, 88, 90, 92-94, 101, 133, and 134. Since the claims of the

Application No. 10/958,999 embrace all limitation of the instant claims, the application claims and the instant claims are obvious variants of one another.

Claims 66, 67, 87-94, 101, 133, and 134 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 29 and 42 of U.S. Patent No. 6,632,671.

The instant claims are drawn to a composition of a plurality of particles comprising a core provided by a bioactive component associated with a surfactant having an HLB value of less than about 6.0, and a shell surrounding the association of the bioactive component and the surfactant, wherein the shell comprises at least one biocompatible polymer and wherein the biocompatible polymer provides specific cellular or tissue uptake; and the particles have an average diameter of less than 50 nm as measured by atomic force microscopy after drying of the particles (claim 66). The biocompatible polymer comprises a macromolecule such as a proteinaceous material (claims 66, 101, 133, and 134), the surfactant has a HLB of less than 5.0 (claim 88) and can be a non-ionic (claim 87) or is selected from the group recited in claim 90, and the composition further comprises a biocompatible oil (claim 92), a water-miscible solvent (claim 93) or a cation selected from the group recited in claim 94. The instant claims embrace the following embodiments: particles with an average diameters of less than 50 nm, the particle comprising bioactive component, a surfactant with an HLB less than 6.0 and a biocompatible polymer that provides specific cellular uptake, wherein the biocompatible polymer is a proteinaceous material such as tenascin.

The patent claims recite a plurality of particles comprising a surfactant with an HLB less than 5.0, a bioactive hydrophobic component (i.e., a bioactive component), and a biocompatible polymer, wherein the particles have an average diameter of less than 50 nm as determined by atomic force microscopy. With respect to the limitation of the biocompatible polymer providing specific cellular uptake, the specification discloses that the biocompatible polymer can be tenascin (see fig. 7B, and also column 3, lines 6-8). The specification discloses that the biocompatible polymer forms a shell surrounding the association of the bioactive component with the surfactant, the hydrophobic bioactive component can be a macromolecule, the particle can further comprise a water-miscible solvent, a biocompatible oil or one of the cations recited in the instant claim 94, the surfactant can be a non-ionic surfactant or 2,4,7,9-tetramethyl-5-decyn-4,7-diol (i.e., a surfactant having an HLB of less than 5.0, the surfactant can be supplied as a mixture of two or more surfactants, the critical micelle concentration can be less than about 200 micromolar (column 3, lines 25-32,column 5, lines 37-52, column 7, lines 38-40, column 9, lines 40-45, column 10, lines 42-66, column 15, lines 30-32). With respect to the limitation of HLB being less than 6.0, the patent claims recite an HLB less than 5.0 that anticipates the claimed HLB of less than 6.0. Therefore, the patent claims 29 and 42 anticipate claims 66, 67, 87-94, 101, 133, and 134 of the instant application. Since the patent claims embrace all the limitation of the instant claims, the application claims and the instant claims are obvious variants of one another.

5. Applicant is advised that should claim 87 be found allowable, claim 90 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). It is noted that claim 90 recites several species of non-ionici surfactants.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 66, 67, 87, 88, 90-92, 94, and 101 are rejected under 35 U.S.C. 102(e) as being anticipated by Unger, E.C. et al. (US Patent No. 6,139,819).

Unger et al. teach particles comprising a core provided by paramagnetic contrast agents, such as Gd^{3+}, Mn^{2+}, or Ni^{2+} that are bound to proteinaceous macromolecules (i.e., a bioactive component comprising a macromolecule), a surfactant molecule, such as cetyl alcohol, which is associated with the bioactive component (i.e., a non-ionic surfactant with HLB less than 5.0), and a biocompatible polymer that ensures

substantial particle encapsulation (i.e., the biocompatible polymer forms a shell that surrounds the association between the bioactive component and the surfactant), wherein the biocompatible polymer can be a protein and wherein the biocompatible polymer provides targeting ligands for targeted delivery to cells or tissues (column 18, line 61, column 55, lines 5-43, column 30, lines 18-32, column 31, lines 29 and 30, column 34, lines 44-49, column 56, lines 1-5). Unger et al. also teach that the particles have a size of about 30nm (column 27, lines 51-53), the particles can comprise a combination of two or more surfactants (column 19, lines 21-25, column 31, lines 52-57), a biocompatible oil, such as peanut oil (column 33, lines 23-25), and a water-miscible solvent (Example 4). Since Unger et al. teach all the limitations of the instant claims, the claimed invention is anticipated by the above-cited art.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 66, 67, 87-94, 101, 133, and 134 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger EC et al., as applied to claims 66, 67, 87, 88, 90-92, 94, and 101 above, in view of Schneider et al. (FEBS Letters, 1998, 429: 269-273).

Unger EC et al. do not teach tenascin or a critical micelle concentration of about 200 micromolar. Schneider et al. teach identification of a polypeptide derived from the

C-terminus of tenascin capable to bind to $\alpha_9\beta_1$ integrins on the cell surface (Abstract, p. 272, column 2 first paragraph and Fig. 4), i.e., Schneider et al. teach a ligand that targets a receptor for tenascin. Schneider et al. also teach their peptide as being suitable to mediate specific gene delivery to $\alpha_9\beta_1$ integrins-expressing cells (Abstract, p. 269, column 2, second paragraph, p. 272, column 2, second and third paragraphs). It would have been obvious to one of skill in the art, at the time the invention was made, to make the particles of Unger et al. by using the peptide of Schneider et al. as targeting moiety with the intent to target the particles to $\alpha_9\beta_1$ integrins-expressing cells, with a reasonable expectation of success. As an alternative, it would have been obvious to one of skill in the art at the time the invention was made, to use tenascin as the proteinaceous biocompatible polymer and targeting agent of Unger et al., with a reasonable expectation of success, since Schneider et al. teach that tenascin is a ligand for $\alpha_9\beta_1$ integrins. The motivation to do so is provided by Schneider et al., who teach $\alpha_9\beta_1$ integrins are highly expressed on human airway epithelia irrespective of any clinical status and therefore targeting this integrin is promising for the development of gene therapy vectors (p. 269, column 1 bridging column 2). One of ordinary skill in the art would have been expected to have a reasonable expectation of success in making such particles because Unger et al. teach that proteins in general can be used for the preparation of their particles and that targeting ligands can also be incorporated into the biocompatible polymer that is part of their particles. With respect to the limitation of the surfactant having a critical micelle concentration of about 200 micromolar, absent evidence of unexpected results, if the general conditions of a given method are

disclosed in the prior art, it would have been obvious to the ordinary skilled artisan to vary the parameters in a given method with the purpose of optimizing the results, i.e., to use a surfactant with the desired critical micelle concentration according to the intended use of the particles. Again, absent evidence to the contrary, it is generally not inventive to discover the optimal working conditions of a prior art method, such conditions can be identified by routine experimentation. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

10. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa

JANET L. EPPS-FORD, PH.D.
PRIMARY EXAMINER